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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,710	07/29/2002	Ray C.J. Chiu	SW A 4338p0090us	2742

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EXAMINER	
KELLY, ROBERT M	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,710	CHIU ET AL.	
	Examiner	Art Unit	
	Robert M Kelly	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 13-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-6, 13-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 July 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments and arguments of 26 July 2004 have been entered.

Claim 2 has been amended.

Claims 1-6 and 13-16 are presently pending.

It is noted that Applicant has, apparently inadvertently, listed claim 17 as previously presented; however, such Claim was cancelled in the Amendments of 1 April 2002; hence, this claim is considered as cancelled.

Claims 1-6 and 13-16 are considered.

Drawings

In light of Applicant's amendments to the drawings, the objection to the drawings is withdrawn.

Claim Objections

In light of Applicant's amendments and arguments of 26 July 2004, the objection to Claim 2 is withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 and 13-16 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, for reasons of record in the Official Action of 24 March 2004, pp. 3-11. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim Rejections - 35 USC § 112 – response to arguments

Applicant's arguments of 26 July 2004 have been fully considered but are not persuasive.

Applicant argues that (i) Chiu (2003) Expert Opin. Biol. Ther., 3(2): 215-25; (ii) an informal list, supplied by Applicant, of clinical trials being performed; (iii) Orlic, et al. (2001) Nature, 410: 701-705; and (iv) Chemdrawy, et al (2002) 124: 584-90 demonstrate a higher state of the art than that shown by the Examiner in the prior Office Action (Applicant's response of 26 July 2004, p. 5, paragraphs 5-6).

Applicant's argument has been considered but is not persuasive. First, Applicant's list of clinical trials does not supply enough information to determine if the methods are the same as Applicant's methods and certainly demonstrate the use of cell other than bone marrow stromal cells (Applicant's response of 26 July 2004, Appendix B). Second, Applicant did not supply the Chemdrawy reference, and the Examiner was unable to obtain a copy, so it was not considered; however, it is also noted that the reference's title indicates the use of myogenic and stem cells, which is not the same as applicant's claimed mesenchymal stem cells. Orlic, although not supplied by Applicant, was obtained the Examiner; however, Orlic is different from Applicant's claimed methods in that not any bone marrow cell was used, but only lineage-negative, c-kit-positive, cells were used (ABSTRACT), and, moreover, Orlic is dated in 2001, after the priority

date of Applicant. Lastly, Chiu does not generally enable Applicant's claimed methods either, but points to the large number of unpredictabilities cited throughout the Official Action of 24 March 2004. Such unpredictabilities include whether such MSC administration would actually reach the tissue and become a functioning part of the tissue, via any particular route of administration, and that such correlates with an improvement of any particular heart condition, or cardiac failure, in particular (e.g., Official Action of 24 March 2004, p. 11, paragraph 4). For example, Chiu begins by stating "Although early Phase I clinical trials have been initiated for both autologous myoblast and autologous marrow cell transplants with favourable reported outcomes, the data are still to preliminary to draw definitive conclusions regarding their safety and efficacy." (ABSTRACT). Hence, Chiu draws doubt to the efficacy of any particular therapy. Moreover, Chiu demonstrates that there is uncertainty in the field with regard to another aspect, that of whether any particular cell type is defined, and whether there exist a single stem cell, or multiple types that may give rise to any particular tissue (p. 216, col. 2). Hence, the Artisan would not be able to reasonably predict that the claimed cells would give rise to the tissue of interest. Emphasizing the point, Chiu points to the fact there exists difficulty in identifying which cells give rise to a particular tissue type, and the difficulty of comparing the results of various published outcomes (p. 217, col. 1, first paragraph), as well as the need for further studies to evaluate the *future* potential of these cell types in therapy (Id., paragraph 2). Homing signals are also not well understood (Id., col. 2, paragraphs 2-3), hence, any particular route of administration would not necessarily be predicted to produce seeding into the tissue of interest. Moreover, others have used cells that have been genetically modified to express Akt (p. 218, last paragraph), but such is not the claimed invention, and Chiu is dated after the priority of the

present application. Still also, Chiu emphasizes that, although Chiu himself believes these cells are not simply the product of fusion, the Artisan may reasonably predict that such fusion is what is seen (p. 221, first paragraph). Lastly, Chiu ends the article with much caution:

> Nevertheless, we have to temper this excitement with caution, lest we repeat the tragedies associated with gene therapy in the last few years. An aggressive and hasty attitude leading to errors could set back the progress of this highly promising therapy for years. Continued active preclinical research, addressing the issues discussed above, will help us to select optimal strategies to use adult stem cell therapy for heart failure, which has the potential of benefiting a vast number of patients.

(p. 221, last paragraph).

Hence, Chiu recognizes that, although the field is promising, much caution is needed because it is still not yet reasonably predictable, for those reasons given above.

Applicant broadly asserts that the two submitted documents above establish the state of the art and level of skill to be much higher than that alleged by the Examiner, and therefore, the invention is enabled (Applicant's response of 26 July 2004, p. 6, first paragraph).

Such is not considered persuasive. As was shown above with regard to Applicant's submitted articles, the stated methods and cells are not always the same as Applicant's claimed methods and cells, and the unpredictabilites are echoed throughout Chiu (See Above, pp. 4-5; e.g., Official Action of 24 March 2004, p. 11, paragraph 4).

Applicant broadly asserts that the application encompasses a wide area of knowledge and that should not prevent the patentability of the claims (Applicant's response of 26 July 2004, p. 6, first paragraph).

Such argument is true, but not persuasive in the present application, because the claims must be enabled, and enabled for their fully-claimed breadth (MPEP 2164.08 [R-2]). If

Applicant's claims were enabled, and enabled for their fully-claimed breadth, they would be patentable over the art of record.

Applicant argues that the Examiner's statement that in view of the articles supplied by Applicant, the art of Li in the Official Action of 24 March 2004, p. 6, is enabling for Applicant's claimed invention (Applicant's response of 26 July 2004, p. 6, paragraph 3).

Such is not persuasive, because Chiu itself indicates that unpredictable nature of the cell types utilized (Chiu, pp. 216-217; Official Action of 24 March 2004, p. 6, paragraph 1), and as such, it is not reasonably predictable that Li's cells are Applicant's cells.

Applicant argues that the Makino reference in the Official Action of 24 March 2004 (p. 4), while demonstrating an immortalized cell line, is enabling for Applicant's invention because Figures 1 and 2 of the instant application demonstrate that Applicant's cells can be used for improving cardiac function, and therefore the Official Action of 24 March 2004 is incorrect (Applicant's response of 26 July 2004, p. 6, paragraph 3).

Such is not persuasive, because, while Applicant has demonstrated the presence of cells, these cells are not demonstrated to improve cardiac function or to even form living, functioning, cardiac tissue (Official Action of 24 March 2004, pp. 10-11, paragraph bridging).

Applicant argues that the numerous clinical trials indicate an expectation of eventual success, and therefore the claims are enabled (Applicant's response of 26 July 2004, p. 7, last paragraph)

Such is not persuasive, because eventual success is not reasonably predictable success, and such success does not necessarily encompass Applicant's taught and claimed methods and cells.

CONCLUSION

No Claim is allowed for reasons of record in the Official Action of 26 July 2004.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert M Kelly whose telephone number is (571) 272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RAM R. SHUKLA, PH.D.
PRIMARY EXAMINER